Marijuana use in adolescence may cause permanent brain abnormalities, study finds

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Regular marijuana use in adolescence, but not adulthood, may permanently impair brain function and cognition, and may increase the risk of developing serious psychiatric disorders such as schizophrenia, according to a recent study from the University of Maryland School of Medicine. Researchers hope that the study, published in *Neuropsychopharmacology*—a publication of the journal *Nature* – will help to shed light on the potential long-term effects of marijuana use, particularly as lawmakers in Maryland and elsewhere contemplate legalizing the drug.

"Over the past 20 years, there has been a major controversy about the long-term effects of marijuana, with some evidence that use in adolescence could be damaging," says the study's senior author Asaf Keller, Ph.D., Professor of Anatomy and Neurobiology at the University of Maryland School of Medicine. "Previous research has shown that children who started using marijuana before the age of 16 are at greater risk of permanent cognitive deficits, and have a significantly higher incidence of psychiatric disorders such as schizophrenia. There likely is a genetic susceptibility, and then you add marijuana during adolescence and it becomes the trigger."

"Adolescence is the critical period during which marijuana use can be damaging," says the study's lead author, Sylvina Mullins Raver, a Ph.D. candidate in the Program in Neuroscience in the Department of Anatomy and Neurobiology at the University of Maryland School of Medicine. "We wanted to identify the biological underpinnings and determine whether there is a real, permanent health risk to marijuana use."

The scientists—including co-author Sarah Paige Haughwout, a research technician in Dr. Keller's laboratory—began by examining cortical oscillations in mice. Cortical oscillations are patterns of the activity of neurons in the brain and are believed to underlie the brain's various functions. These oscillations are very abnormal in schizophrenia and in other psychiatric disorders. The scientists exposed young mice to very low doses of the active ingredient in marijuana for 20 days, and then allowed them to return to their siblings and develop normally.

"In the adult mice exposed to marijuana ingredients in adolescence, we found that cortical oscillations were grossly altered, and they exhibited impaired cognitive abilities," says Ms. Raver. "We also found impaired cognitive behavioral performance in those mice. The striking finding is that, even though the mice were exposed to very low drug doses, and only for a brief period during adolescence, their brain abnormalities persisted into adulthood."

The scientists repeated the experiment, this time administering marijuana ingredients to adult mice that had never been exposed to the drug before. Their cortical oscillations and ability to perform cognitive behavioral tasks remained normal, indicating that it was only drug exposure during the critical period of adolescence that impaired cognition through this mechanism. The researchers took the next step in their studies, trying to pinpoint the mechanisms underlying these changes and the time period in which they occur.

"We looked at the different regions of the brain," says Dr. Keller. "The back of the brain develops first, and the frontal parts of the brain develop during adolescence. We found that the frontal cortex is much more affected by the drugs during adolescence. This is the area of the brain controls executive functions such as planning and impulse control. It is also the area most affected in schizophrenia."

Dr. Keller's team believes that the results have indications for humans as well. They will continue to study the underlying mechanisms that cause these changes in cortical oscillations. "The purpose of studying these mechanisms is to see whether we

can reverse these effects," says Dr. Keller. "We are hoping we will learn more about schizophrenia and other psychiatric disorders, which are complicated conditions. These cognitive symptoms are not affected by medication, but they might be affected by controlling these cortical oscillations."

"This study is an example of how the basic science research taking place in our state-of-the-art laboratories can impact human health and inform health policy," says E. Albert Reece, M.D., Ph.D., M.B.A., Vice President for Medical Affairs at the University of Maryland and John Z. and Akiko K. Bowers Distinguished Professor and Dean of the University of Maryland School of Medicine. "We are proud of this groundbreaking discovery and look forward to watching this research develop further."

Provided by University of Maryland

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